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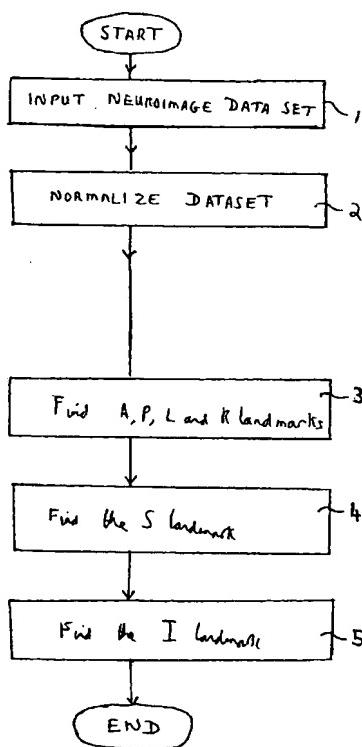
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(54) Title: AUTOMATED METHOD FOR IDENTIFYING LANDMARKS WITHIN AN IMAGE OF THE BRAIN

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(57) Abstract: A method is disclosed for obtaining the location of a landmark in an MR image of a brain. In a first step, a region of interest in a plane within the MR image containing the landmark is defined. In a second step, the ROI is binarised into foreground and background voxels based on at least one threshold selected using anatomical knowledge. In a third step a set of object voxels is identified from the foreground voxels, excluding voxels which were only classified as object due to proximity of cortical and non-cortical structures. This can be done by morphological processing which reclassifies voxels which may have been incorrectly classified as object, followed by restoring voxels due to the partial volume effect and/or morphological erosion/opening. In a fourth step, an automatic process is then carried out to identify one or more landmarks in the modified binarised image.



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Automated Method for identifying landmarks within an image of the brainField of the invention

The present invention relates to methods for automatically identifying landmarks within images of a brain.

5 Background of Invention

- The Talairach transformation is widely used for analysis of neurological images. It involves identifying eight landmarks, which are used to define a coordinate system. The Talairach landmarks subdivide the brain into 12 cuboids, and the Talairach transformation is to warp the images within each cuboid linearly. In this way the brain images are normalised by a three-dimensional piece-wise linear warping. This scheme has several applications, in particular because it makes it possible to compare neurological images from different individuals. One improvement on this scheme, while following its conceptual rationale, is the improvement of the definitions of the landmarks, to give "modified Talairach landmarks" (as defined in the article "Modified Talairach Landmarks", W. L. Nowinski, Acta Neurochirurgica, 2001, 143, p1045-1057, the disclosure of which is incorporated herein by reference).
- 10 A principal advantage of the Talairach transform is its simplicity. Although numerous non-linear image registration techniques are known, in principle providing a higher accuracy, the non-linear techniques have limitations which make them difficult to use beyond a research environment. In particular, a prohibitively high computational time is required. Whereas the Talairach transformation can be performed in less than a second in a standard personal computer, some non-linear methods require days of computation. More fundamentally, the non-linear methods are conceptually complex, and must be treated as "black boxes", which limits their clinical acceptance.
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- 20
- 25

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Furthermore, there is no established methodology for validation of the non-linear registration techniques.

One drawback of the Talairach transformation, however, is that the  
5 identification of the landmarks has not so far been automated reliably, so that  
when using conventional software which employs the Talairach transformation  
the landmarks still have to be identified by user interaction (e.g. R. W. Cox,  
"AFNI: Software for Analysis and Visualization of Functional Magnetic  
Resonance Neuroimages", Computer and Biomedical Research, 1996, 29,  
10 p162-173). Quite apart from the time the interactive identification of the  
landmarks takes, different individuals are liable to locate the landmarks in  
slightly different positions, which reduces the robustness of the method.

#### Summary of the Invention

15 The present invention aims to provide new and useful techniques and  
apparatus for identifying automatically landmarks within neurological images,  
and in particular the Talairach landmarks or modified Talairach landmarks.

20 The invention makes use of the concepts "foreground voxels" and  
"background voxels". "Binarising" a set of voxels means to divide the voxels  
into these two categories.

25 Furthermore, certain voxels are "object voxels". Object voxels are voxels in a  
location which corresponds to a physical identity (cerebral structure), such as,  
in the context of this invention, the union of grey matter and white matter.

In general terms, the invention proposes that the location of one or more  
landmarks is obtained by the following steps:

- (a) a region of interest in a plane within an MR image of a brain and containing the landmark(s), is identified;
  - (b) the region of interest is binarised into foreground and background voxels based on at least one threshold selected using anatomical knowledge,
- 5       (c) a set of object voxels is identified from the foreground voxels, excluding voxels which were only classified as foreground voxels due to proximity of cortical and non-cortical structures,
- (d) object voxels are identified from the background voxels due to the partial volume effect and morphological erosion/opening, and
- 10     (e) an automatic process is then carried out to identify one or more landmarks in the modified binarised image.

The step of reclassifying voxels may be performed in two stages: (i) a first stage of morphological processing, and (ii) a second step of restoring voxels which have been incorrectly reclassified in the morphological processing.

- 15 Anatomical knowledge may also be used in the reclassifying step, e.g.. by using the expected shapes of cortical and/or non-cortical structures to modify the classification.

The threshold is preferably selected by the steps of:

- 20 (i) using prior knowledge about the image to derive an intensity range of voxels in the said region of interest;
- (ii) obtaining a frequency distribution of the intensities within the said intensity range of voxels within the said region of interest; and
- (iii) using the said frequency distribution to derive the threshold.

The intensity threshold may be selected by minimising a function which is a sum of the variances of the intensities below and above the threshold.

Optionally, this function may be a weighted sum defined based on two constants  $W_1$  and  $W_2$ . This is referred to here as a "range constrained weighted variance method".

For example, labelling the possible values of voxel intensity by an integer index  $i$  and their respective frequencies by  $h(i)$ , and writing the lower and upper intensities respectively as  $r_{low}$  and  $r_{high}$ , the weighted sum is given by

$$\theta_{RCLWW} (W_1, W_2) = \max_{r} (\Pr(C_1)D(C_1)W_1 + \Pr(C_2)D(C_2)W_2),$$

where  $\Pr(\cdot)$  denotes the class probability ( $\Pr(C_1) = \sum_{i=r_{low}}^n h(i)$  and

$$\Pr(C_2) = \sum_{i=r_{high}+1}^{r_{high}} h(i)),$$

$$D(C_1) = (\mu_0 - \mu_T)^2 \text{ and } D(C_2) = (\mu_1 - \mu_T)^2, \quad \text{where} \quad \mu_T = \sum_{i=r_{low}}^{r_{high}} i \times h(i),$$

$$\mu_0 = \sum_{i=r_{low}}^n i \times h(i) \text{ and } \mu_1 = \sum_{i=r_{high}+1}^{r_{high}} i \times h(i).$$

The steps (a) to (d) may be performed repeatedly for different landmarks. One or more landmarks may be located for each of the starting planes of the MR image.

In the case of identifying the I landmark (which is a position on a coronal plane) the left and right halves of the brain may be treated partly separately, such that the I landmark is identified using the half of the brain which appears to have been segmented more accurately.

The invention may be expressed as a computer-implemented method, or alternatively as a computer system arranged to perform such a method.

Brief Description of The Figures

Preferred features of the invention will now be described, for the sake of illustration only, with reference to the following figures in which:

Fig. 1 is a flow chart of a method which is an embodiment of the  
5 invention;

Fig. 2 is a flow chart showing in more detail sub-steps of step 3 of the flow chart of Fig. 1;

Fig. 3, which is composed of Figs. 3(a) to 3(d), shows an example of performing the steps to identify the A, P, L and R landmarks in the method of  
10 Fig. 1;

Fig. 4, which is composed of Figs. 4(a) to 4(d), shows an example of performing the steps to identify the S landmark in the method of Fig. 1; and

Fig. 5, which is composed of Figs. 5(a) to 5(d), shows an example of performing the steps to identify the I landmark in the method of Fig. 1  
15

Detailed Description of the embodiments

Referring firstly to Fig. 1, the steps of a method which is an embodiment of the invention are shown.

In step 1, a dataset which is a neuroimage (i.e. an image of a brain) is loaded.  
20 This image is a three dimensional data, typically obtained from a number of scans in different respective planes.

From this data, the midsagittal plane (MSP) is determined. This is preferably done using the method disclosed in WO02/069827, "Method and apparatus for determining symmetry in 2D and 3D images"; by Hu and Nowinski (the disclosure of which is incorporated herein by reference). However, the invention is not limited in this respect, and any other technique for determining  
25

the MSP may also be applied. Indeed, it would also be possible within the scope of the invention for the input data to specify the MSP.

The coordinates of the anterior commissure (AC) and posterior commissure (PC) are then determined automatically. This can be done by the method disclosed in WO02/43003, "Methods and apparatus for processing medical images", by Nowinski and Thirunavuukarasuu (the disclosure of which is incorporated herein by reference), although once more the invention is not limited in this respect.

10

In step 2 of Fig. 1, the data is normalised to occupy a predefined gray-scale range. According to the standard radiological convention, we write the coordinate system as  $(x,y,z)$ , where the x-axis is from the subject's right to left, the y-axis is from anterior to posterior, and z from superior to inferior. Thus, an xz-plane is a coronal plane, a yz-plane is a sagittal plane, and an xy-plane is an axial plane. Let  $g(x,y,z)$  denote the gray level of the input data at a voxel at position  $(x,y,z)$ , and let  $g_0$  and  $g_1$  denote the grey levels such that one percent of the voxels have an intensity less than  $g_0$  and one percent of the voxels have an intensity greater than  $g_1$ . Then, we obtain a normalised gray level

15      20       $\hat{g}(x,y,z)$  which, for a given position  $(x,y,z)$  is given by:

$$\begin{aligned}\hat{g}(x,y,z) &= 0 && \text{if } g(x,y,z) \leq g_0 \\ \hat{g}(x,y,z) &= \frac{g(x,y,z) - g_0}{g_1 - g_0} && \text{if } g_0 < g(x,y,z) < g_1 \\ \hat{g}(x,y,z) &= 255 && \text{if } g(x,y,z) \geq g_1\end{aligned}$$

25

Each slice of the normalised data has its own co-ordinate system  $(u,v)$  where  $u$  is the horizontal direction and  $v$  is the vertical direction.

In step 3, the position of the A, P, L and R landmarks is located. This is done by the series of steps shown in Fig. 2.

Firstly, in step 3.1 a region of interest (ROI) is defined. These may be the voxels within the skull. These voxels can be determined by the following  
5 steps:

- (a) A histogram-based thresholding method is used to binarise the AP plane (as used for example in M. E. Brummer, R. M. Mersereau, R. L. Eisner, R.J. Lewine, "Automatic detection of brain contours in MRI data sets", IEEE Transactions on Medical Imaging 1993; 12(2), p153-166).
- 10 (b) A morphological closing operation is performed using a 3x3 structuring element (SE) to connect small gaps in the ROI.
- (c) The largest connected component is identified, and the holes within the component are filled.

Fig. 3(a) shows the AP plane in a typical example of the use of this method.  
15 Fig. 3(b) shows the corresponding ROI.

In step 3.2 an optimum threshold is determined, based on the range-constrained weighted variance thresholding method. This includes following steps, which are explained in a separate patent application by two of the present inventors: "Methods and apparatus for binarizing images", Singapore  
20 patent application 200307531-4, by Q. M. Hu, Z. Hou, and W.L. Nowinski, which was still unpublished at the priority date of the present application, and the disclosure of which is incorporated by reference.

Firstly, prior knowledge of the image is used to define an ROI which is a subset of the image. This process can be done by whatever means, either  
25 automatic, semi-automatic, or even manual. Then an analysis is performed on

the frequency of occurrence of intensities within the ROI, and a range of frequencies is defined, again using prior knowledge.

For example, without losing generality, we denote the image to be processed as  $f(x)$ , where  $f(x)$  is the gray level at a voxel labelled  $x$ . It is further supposed that the processed image has  $L$  gray levels denoted by  $r_i$ , where  $i$  is an integer in the range 0 to  $L-1$  and  $r_0 < r_1 < \dots < r_{L-1}$ . It is also assumed that the object of interest has higher intensity values than the background. Suppose that due to prior knowledge or test we know that the proportion of the ROI which is occupied by the object is in the percentage range  $per_0$  to  $per_1$ .

Let  $h(i)$  denote the frequency of gray level  $r_i$ , and let  $H(i)$  denote the cumulative frequency which is  $\sum_{i'=0}^i h(i')$ , where  $i'$  is an integer dummy index. Considering two values of  $i$  written as  $m$  and  $n$ , the frequency of intensities in the range  $r_m$  to  $r_n$  is  $\sum_{i=m}^n h(i')$ . Thus, we can use  $per_0$  to calculate a gray level  $r_{low}$ , such that we are sure that all the voxels having lower intensity represent background.  $r_{low}$  can be written as:

$$r_{low} = \min_i \{i \mid H(i) \geq per_0\}. \quad (1)$$

Similarly, we can use  $per_1$  to calculate a gray level  $r_{high}$  such that we are sure that all voxels having higher intensity represent the object:

$$r_{high} = \min_i \{i \mid H(i) \geq per_1\}. \quad (2)$$

Let  $r_k$  fall within the range  $r_{low}$  to  $r_{high}$ , and suppose that the voxels of the ROI are in two classes  $C_1$  and  $C_2$ , where  $C_1$  is voxels of the background class and consists of voxels with gray levels  $r_{low}$  to  $r_k$ , and  $C_2$  is voxels of the object class and is composed of voxels with gray levels  $r_k+1$  to  $r_{high}$ . The range-constrained

weighted variance thresholding method maximises the "weighted between-class variance" defined as:

$$\theta_{RCWV}(W_1, W_2) = \max_n (\Pr(C_1)D(C_1)W_1 + \Pr(C_2)D(C_2)W_2),$$

- where  $W_1$  and  $W_2$  are two positive constants selected by the user and  
5 representing the weights of the two respective class variances,  $\Pr(\cdot)$  denotes the class probability; i.e.

$$\Pr(C_1) = \sum_{i=r_{low}}^n h(i), \quad \Pr(C_2) = \sum_{i=r_k+1}^{r_{high}} h(i),$$

and  $D(C_1)$  and  $D(C_2)$  are given by:

$$D(C_1) = (\mu_0 - \mu_T)^2 \text{ and } D(C_2) = (\mu_1 - \mu_T)^2, \text{ where } \mu_T = \sum_{i=r_{low}}^{r_{high}} i \times h(i),$$

10  $\mu_0 = \sum_{i=r_{low}}^n i \times h(i) \text{ and } \mu_1 = \sum_{i=r_k+1}^{r_{high}} i \times h(i).$

When  $W_1$  is bigger than  $W_2$ , background homogeneity is emphasised.

Step 3.2 may be done by specifying  $per_0$  and  $per_1$  to be 14% and 28% respectively. The optimum threshold is denoted as  $\theta_1$ .

- In step 3.3, we segment the AP plane by assigning voxels to foreground if  
15 they are bigger than  $\theta_1$ , and otherwise assigning them to background. The binarised image is denoted as BWAP1(u,v).

In steps 3.4 we reclassify the voxels: firstly by a morphological processing, then processing using anatomical knowledge, and finally performing a restoring step.

- 20 The sub-steps of the morphological processing and processing using anatomical knowledge are as follows:
- (a) A distance transform of the ROI is performed using the 2-3 metric (in this metric the distances between any two voxels is determined by defining

- the shortest path of voxels between them, and adding the distance increments along this path. The distance increments between two voxels which are nearest neighbours in a direction parallel to one of the axes (4-connected nearest neighbours) is taken as 2, and the distance between two voxels which
- 5 are nearest neighbours diagonally (8-connected nearest neighbours) is taken as 3) and the distance codes are converted into distance indices by the method of Hu Q.M., "Two and three-dimensional skeletonization", WO 02/058008). The maximum distance index is denoted as maxDSkull.
- (b) A morphological opening operation is performed with a 3x3 SE with
- 10 respect to BWAP1(u, v), to obtain BWAP2(u,v).
- (c) A morphological opening operation is performed with a 5x5 SE with respect to BWAP1(u,v) to obtain BWAP3(u,v).
- (d) The foreground components of BWAP3(u,v) are found. For each foreground component, its minimum and maximum distance indices are
- 15 denoted as minD and maxD respectively. A foreground component is treated as an object component when maxD-minD is bigger than a value (e.g. 20) or maxD is bigger than a second value (e.g. maxDSkull/2).
- (e) The object voxels are excluded from the foreground voxels of BWAP2(u,v). The connected foreground components of BWAP2(u;v) are
- 20 found. The number of voxels of each foreground component are denoted as nosVoxel. A foreground component of BWAP2(u,v) is categorised as an object component only when the shape of the component is not similar to meninges. According to anatomical knowledge, meninges have a shape similar to the skull and are quite thin. So, when maxD-minD is smaller than
- 25 0.1\*nosVoxel, the component is highly likely to be a meninges. Otherwise, it is classified as an object component.

The lost object voxels are restored by the following steps:

- (a) Object voxels far from the skull lost due to the morphological opening operation are restored. This is achieved by checking the non-object voxels with a distance index greater than  $\text{maxDSkull}/4$ . If their gray level is bigger than  $\theta_1$ , the voxels are reclassified as object voxels.
- 5 (b) Object voxels around the boundaries lost due to the morphological opening operation are restored. For each object boundary voxel (an object boundary voxel is an object voxel having at least one non-object voxel as one of its 8 immediate neighbours), each of its 8 immediate neighbours is reclassified as an object voxel if its grey level is greater than  $\theta_1$ .
- 10 Note that this restoration is not performed around the most anterior (i.e. minimum v) and most posterior (i.e. maximum v) parts of the straight line connecting AC and PC, to avoid the sinus and meninges. Specifically, suppose the maximum and minimum v coordinates of object voxels are  $\text{minVap}$  and  $\text{maxVap}$  respectively, and denote the coordinates of AC on the
- 15 AP plane as  $(\text{acUap}, \text{acVap})$  and the coordinates of the PC on the AP plane as  $(\text{pcUap}, \text{pcVap})$ . The restoration is not carried out in the following two regions:
- $$|u-\text{acUap}|<10\text{mm} \text{ and } |v-\text{minVap}|<3\text{mm}. \quad (3)$$
- $$|u-\text{pcVap}|<10\text{mm} \text{ and } |v-\text{maxVap}|<3\text{mm}, \quad (4)$$
- where  $|x|$  stands for the absolute value of x.
- 20 (c) Object voxels (that is, all voxels which are physically either GM or WM) lost due to the partial volume effect are restored. Since the statistics of GM, WM, CSF, air, meninges and bones are not available, the partial volume effect is alleviated by reducing the threshold by 10. That is, for any object boundary voxel, each of its immediate 8 neighbours is re-classified as an object voxel if
- 25 its gray level is bigger than  $(\theta_1-10)$ . The restoration is not carried out in the two regions defined by formulae (3) and (4).

In step 3.5, the minimum and maximum v coordinates of the object voxels are taken respectively as the v coordinates of the A and P landmarks respectively. Similarly, the minimum and maximum u coordinates of the object voxels are taken as the u coordinates of the L and R landmarks respectively. Note that

5 the u-coordinate in the AP plane corresponds to the x-coordinate of the three-dimensional volume, and the v-coordinate in the AP plane corresponds to the y-coordinate in the three-dimensional volume.

Figs. 3(c) and 3(d) show the segmented AP plane, and the 4 landmarks overlaid over it. The white horizontal lines show the v coordinates of the A and  
10 P landmarks, while the white vertical lines shown the u coordinates of the L and R landmarks on the AP plane.

In step 4 of Fig. 1, we determine the position of the S landmark. The VPC plane is a coronal slice perpendicular to both the MSP and the AP plane, and it passes through the PC. To determine the position of the S landmark, we  
15 only need to determine its v co-ordinate. The v coordinate of the S landmark is the smallest v coordinate of all the cortical voxels on the VPC plane. The S landmark is localized by segmentation of a virtual slice aVPC(u,v) with the close skull.

The VPC plane is denoted as VPC(u,v), the coordinates of the PC within  
20 VPC(u,v) are denoted as (pcU, pcV).

In step 4.1, a virtual plane aVPC(u,v) is constructed in the following way:

(a) aVPC(u,v) = VPC(u,v) when v is not bigger than pcV.

(b). aVPC(u,v) =VPC(u,2pcV-v) when v is bigger than pcV and smaller than 2pcV.

25 Figs. 4(a) and 4(b) show a VPC and the corresponding virtual slice aVPC.

In step 4.2, the ROI corresponding to aVPC is found. This procedure is done in the same way in which the ROI for the AP plane was found above (step 4.1 above).

- In step 4.3, the optimum threshold  $\theta_2$  is determined by the range-constrained
- 5 weighted thresholding method, by specifying per<sub>0</sub> and per<sub>1</sub> to be 20% and 40% respectively.

In step 4.4, the aVPC plane is segmented using the optimum threshold  $\theta_2$ , by the same set of sub-steps explained in step 4.3 above.

- In step 4.5, the threshold  $\theta_2$  is adjusted using anatomical knowledge. Since
- 10 the vertical line passing through the PC in the vicinity of the S landmark should be interhemispheric fissure voxels,  $\theta_2$  should be higher than the gray levels of voxels on the vertical line segment starting from 2mm above and ending 2mm below the object voxels with the minimum v coordinate found in step 4.4. If  $\theta_2$  is indeed bigger than this value, then it is not changed.
- 15 However, if it is lower, it is modified to be 5 plus the maximum gray level of the line segment, and the aVPC(u,v) is re-segmented with the modified threshold  $\theta_2$ , by the same sub-steps as those used to segment the AP plane in step 4.3 above, including the same morphological opening operations.

In step 4.6, lost object voxels are restored. This is done by the following steps:

- 20 (a) Object voxels around the object boundaries lost due to the morphological opening operation are restored. This is done by, reclassifying an non-object voxel which has an object boundary voxel as a nearest neighbour and which has a gray level greater than  $\theta_2$ .

- Note, however, that to avoid the sinus/meninges, the restoration is not carried
- 25 out in the region defined by:

$$|u - pcU| < 10\text{mm} \text{ and } |v - \text{minVavp}| < 3\text{mm} \quad (5)$$

where  $\text{minVavp}$  denotes the minimum  $v$  coordinate of object voxels.

- (b) Object voxels lost due to the partial volume effect are restored. This is done by reclassifying an non-object voxel having an object boundary voxel as
- 5 a nearest neighbour and which has a gray level higher than  $(\theta_2 - 10)$ . The restoration is not, however, carried out in the region defined by equation (5).

The segmented aVPC after restoration sub-steps (a) and (b) is shown in Fig. 4(c).

- 10 In step 4.7, the  $v$  coordinate of the S landmark is the mimimum  $v$  coordinate of all object voxels in aVPC. The  $v$  coordinate of S in the aVPC plane is equal to its  $z$  coordinate in the full three-dimensional volume.

Fig. 4(c) shows the segmented aVPC slice, and Fig. 4(d) shows the original VPC overlaid by a horizontal line indicating the  $z$  coordinate (or equivalently  $v$  coordinate) of the S landmark.

- 15 In step 5, the position of the I landmark is determined. The VAC plane is a coronal slice parallel to the VPC plane, and passes through the AC. Only the  $v$  coordinate of the I landmark is need, and it is the maximum  $v$  coordinate of all the cortical voxels on the VAC plane. It is determined by segmenting the VAC plane directly constrained by anatomical knowledge. It is assumed that
- 20 the maximum difference in the  $z$ -coordinate between the AC and the I landmark is no more than 50mm. We denote that coordinates of the AC in the VAC( $u, v$ ) by  $(acU, acV)$ .

Specifically, the I landmark is obtained by the following sub-steps:

In step 5.1,  $VAC(u,v)$  is binarised by assigning all voxels with gray levels bigger than  $\theta_2$  to be foreground voxels, and the rest as background voxels. The binarised image is denoted as  $BWVAC1(u,v)$ .

- In step 5.2, the region around the AC is connected to make subsequent "seeding" feasible. Here "seeding" means to find connected components from a specified voxel ("seed") with all the voxels in the component being of the same type (i.e. background, foreground or object). The region around the AC is connected by setting the  $BWVAC1(u,v)$  to foreground when  $|v-acV|$  is smaller than 3mm.
- 10 Step 5.3 employs a vertical line passing through the AC to separate the VAC into left and right halves. The voxels on the vertical line with a v-coordinate greater than  $acV+3mm$  are set to background. That is,  $BWVAC1(u,v)$  is set to background when  $v$  is bigger than ( $acV+3mm$ ) and  $u$  is equal to  $acU$ . This has the effect that there is foreground separation in the neck region.
- 15 In step 5.4, a morphological opening operation is performed on  $BWVAC1(u,v)$  using a 3x3 SE, to give  $BWVAC2(u,v)$ . This operation breaks weak connections between the cortex and the skull and between the cortex and the neck.
- 20 In step 5.5, a morphological erosion operation is performed using a 3x3 SE, to give  $BWVAC3(u,v)$ . This operation further breaks the connections between the cortex and the skull and between the cortex and the neck.
- In step 5.6, we seed from ( $acU, acV$ ), to obtain the foreground component. Then, we perform a morphological dilation on the seeded foreground component with a 3x3 SE, to obtain  $BWVAC4(u,v)$ . The serial operations (erosion followed by seeding and dilation) are intended to break strong connections between the cortex and the skull, and between the cortex and the neck, while retaining the original shape of the cortex.

In step 5.7, the maximum value of v for which a foreground BWVAC4(u,v) voxel exists having u smaller than acU, is found, and denoted as maxVL.

In step 5.8, the maximum value of v for which a foreground BWVAC4(u,v) voxel exists having u not less than acU, is found, and denoted as maxVR.

5 In step 5.9, the left half of BWVAC4 (u,v) (i.e. the values of u smaller than acU) is restored in two substeps if (maxVL-acV) is smaller than 50mm:

(a) Firstly, the effects of the morphological opening operation are counteracted, by changing any background voxel which has at least a foreground voxel of BWVAC4(u,v) as one of its 8 immediate neighbours and

10 which has a gray level in VAC(u,v) greater than  $\theta_2$  to foreground.

(b) Secondly, the effects of the partial volume effect are counteracted by restoring any background voxel which has a foreground boundary voxel (a foreground boundary voxel is a foreground voxel, within its 8 immediate neighbours there is at least a background voxel) of BWVAC4(u,v) as one of its

15 8 immediate neighbours and which has a gray level in VAC(u,v) bigger than ( $\theta_2 - 10$ ) to foreground.

Similarly, the right half of BWVAC4(u,v) (i.e. the half with u not less than acU) is restored by two corresponding steps when maxVR-acV is smaller than 50mm.

20 Object voxels are all foreground voxels in this case.

In step 5.10, if both (maxVL-acV) and (maxVR-acV) are smaller than 50mm, the v coordinate of the I landmark is obtained as the v component of the object voxel in BWVAC4(u,v) with the biggest value of v. If one of (maxVL-acV) or (maxVR-acV) is smaller than 50mm and the other is not, the v-

25 coordinate of the I landmark is obtained as the maximum v coordinate of all the object voxels from the side (i.e. the left side or right side) for which the

maximum v coordinate of the object voxels is smaller than (50+acV). If both of (maxVL-acV) and (maxVR-acV) are bigger than 50mm, the v coordinate of the I landmark is the maximum v coordinate of all the object voxels on the side (i.e. left or right) whose maximum object v coordinate is smaller. Note 5 that the v coordinate of BWVCA(u,v) corresponds to the z coordinate of the dataset.

Fig. 5(a) shows the original VAC, Fig. 5(b) shows the binarised VAC (i.e. BWVAC1), Fig. 5(c) shows the processed foreground (BWVAC4), and Fig. 5(d) shows the v coordinate (or equivalently z coordinate) of the I landmark 10 overlaid on the original VAC plane.

Note that the set of sub-steps performed in steps 4 and 5 can be considered as corresponding to those shown in Fig. 2 for finding the A, P, L and R landmarks. That is, a ROI is identified; a threshold is selected (or, in the case of step 5, the threshold used is that same one derived in step 4); a 15 segmentation is performed; then a reclassification is performed; and finally the landmarks are identified.

Although only a single embodiment of the invention has been described in detail, many variations are possible within the scope of the invention as will be clear to a skilled reader.

Claims

1. A computer-based method for locating one or more landmarks using an MR image of a brain, the method including the following automatic steps:
  - (a) identifying a region of interest with a plane of the MR image, the plane containing the landmark(s);  
5
  - (b) binarising the plane of the MR image into foreground and background voxels based on at least one threshold selected using anatomical knowledge;
  - (c) identifying a set of object voxels from the foreground voxels, the set  
10 of object voxels excluding voxels which were only classified as foreground voxels due to proximity of cortical and non-cortical structures;
  - (d) identifying object voxels from the background voxels due to the partial volume effect and/or morphological erosion/opeing; and
  - (e) identifying the one or more landmarks using the object voxels.  
15
2. A method according to claim 1 in which the step of identifying the object voxels is performed in two stages:
  - (i) morphological processing which excludes foreground voxels which may not be object voxels, and
  - (ii) restoring voxels which have been incorrectly excluded in the  
20 morphological processing.
3. A method according to claim 2 in which the step of identifying the object voxels further includes applying anatomical knowledge to identify the object voxels.

4. A method according to claim 3 in which the anatomical knowledge is knowledge about the expected shapes of cortical and/or non-cortical structures.
5. A method according to any preceding claim in which the threshold is selected by the steps of:
- (i) using prior knowledge about the image to derive an intensity range of voxels in the said region of interest; and
  - (ii) obtaining a frequency distribution of the intensities within the said intensity range of voxels within the said region of interest; and
- 10 (iii) using the said frequency distribution to derive an intensity threshold.
6. A method according to claim 5 in which the intensity threshold is selected by minimising a function which is a sum of the variances of the intensities below and above the threshold.
7. A method according to claim 6 in which said function is a weighted sum defined based on two constants  $W_1$  and  $W_2$ .
- 15 8. A method according to claim 7 in which, labelling the possible values of voxel intensity by an integer index  $i$  and their respective frequencies by  $h(i)$ , and writing the lower and upper intensities respectively as  $r_{low}$  and  $r_{high}$ , the weighted sum is given by
- 20  $\theta_{RCLWW} (W_1, W_2) = \max_n (\Pr(C_1)D(C_1)W_1 + \Pr(C_2)D(C_2)W_2),$
- where  $\Pr(\cdot)$  denotes the class probability ( $\Pr(C_1) = \sum_{i=r_{low}}^n h(i)$  and  $\Pr(C_2) = \sum_{i=r_{high}+1}^{r_{high}} h(i)$ ), and  $D(C_1)$  and  $D(C_2)$  are given by:

$$D(C_1) = (\mu_0 - \mu_T)^2 \text{ and } D(C_2) = (\mu_1 - \mu_T)^2, \quad \text{where} \quad \mu_T = \sum_{i=r_{\text{low}}}^{r_{\text{high}}} i \times h(i),$$

$$\mu_0 = \sum_{i=r_{\text{low}}}^k i \times h(i) \text{ and } \mu_1 = \sum_{i=r_k+1}^{r_{\text{high}}} i \times h(i).$$

9. A method according to any of claims 1 to 8 in which the set of steps (a) to (e) are performed repeatedly, in each set of steps identifying at least one  
5 corresponding landmark.

10. A method according to any of claims 1 to 8 in which the set of steps (a) to (d) are performed to locate the A, P, L and R landmarks,

in step (a) the region of interest being defined within the AP plane; and

10. A method according to any of claims 1 to 8 in which the set of steps (a) to (d) are performed to locate the A, P, L and R landmarks,  
15 in step (e) the most anterior and most posterior of the object voxels being taken respectively as the vertical coordinates of the A and P landmarks respectively, and the extreme horizontal components of the object voxels are taken as the horizontal coordinates of the L and R landmarks respectively.

11. A method according to claim 10 in which in step (c):

15. A method according to claim 10 in which in step (c):  
at least one morphological opening operation on the binarized image obtained in step (b) is performed; and

one or more voxels of the image(s) obtained by the opening operation(s) are classified as object voxels or otherwise according to at least one criterion based on distances in the image(s) obtained by the opening operation(s) and anatomical knowledge.

20. 12. A method according to claim 11 in which, prior to the classification, a maximum distance maxDSkull is obtained from a distance transform of the ROI.

13. A method according to claim 11 in which, in the classification:

object voxels far from the skull lost due to the morphological opening operation(s) are restored

object voxels around the boundaries lost due to the morphological opening operation(s) are restored; and

- 5 object voxels lost due to the partial volume effect are restored.

14. A method according to any of claims 1 to 8 in which the set of steps (a) to (d) are performed to obtain the S landmark,

in step (a) the region of interest being defined within a virtual plane obtained from the VPC coronal slice;

- 10 in step (e) the position of the S landmark is the most superior point within the object voxels.

15. A method according to claim 14 in which in step (c):

at least one morphological opening operation on the binarized image obtained in step (b) is performed;

- 15 one or more voxels of the image(s) obtained by the morphological opening operation(s) which are not presently classified as object voxels are re-classified as object voxels if they are one of the eight immediate neighbours of an object voxel and if their intensity value in the MR image is higher than a value defined in relation to a second threshold.

- 20 16. A method according to any of claims 1 to 8 in which the set of steps (a) to (d) is performed to identify the I landmark,

in step (a) the region of interest being defined within the VAC plane;

in step (e) the I landmark being defined as the most inferior point within the object voxels.

17. A method according to claim 16 in which the threshold is obtained during a preceding process according to claim 1 of locating the S landmark.
18. A method according to claim 16 or claim 17 in which, in step (c), (i) at least one morphological opening operation and/or (ii) at least one seeding operation, are performed on the binarized image obtained in step (b).
19. A method according to claim 18 in which, in step (c), one or more voxels of the image(s) obtained by the morphological opening operation(s) which are not presently classified as object voxels are re-classified as object voxels if they are one of the eight immediate neighbours of an object voxel and if their intensity value in the MR image is higher than a value defined in relation to a second threshold.
20. A method according to claims 16 to 19 in which the left and right halves of the brain are treated separately, and the object voxels used to obtain the location of the I landmark relate to a selected half of the brain, the selected half of the brain having been selected based on a predefined criterion.
21. A system for locating one or more landmarks using an MR image of a brain, the system including:
  - an interface to receive data encoding the MR image; and
  - a processor arranged to perform the following steps:
    - (a) identifying a region of interest with a plane of the MR image, the plane containing the landmark(s);
    - (b) binarising the plane of the MR image into foreground and background voxels based on at least one threshold selected using anatomical knowledge;

- (c) identifying a set of object voxels from the foreground voxels, the set of object voxels excluding voxels which were only classified as foreground voxels due to proximity of cortical and non-cortical structures;
- 5 (d) identifying object voxels from the background voxels due to the partial volume effect and/or morphological erosion/opeing; and
- (e) identifying the one or more landmarks using the object voxels.

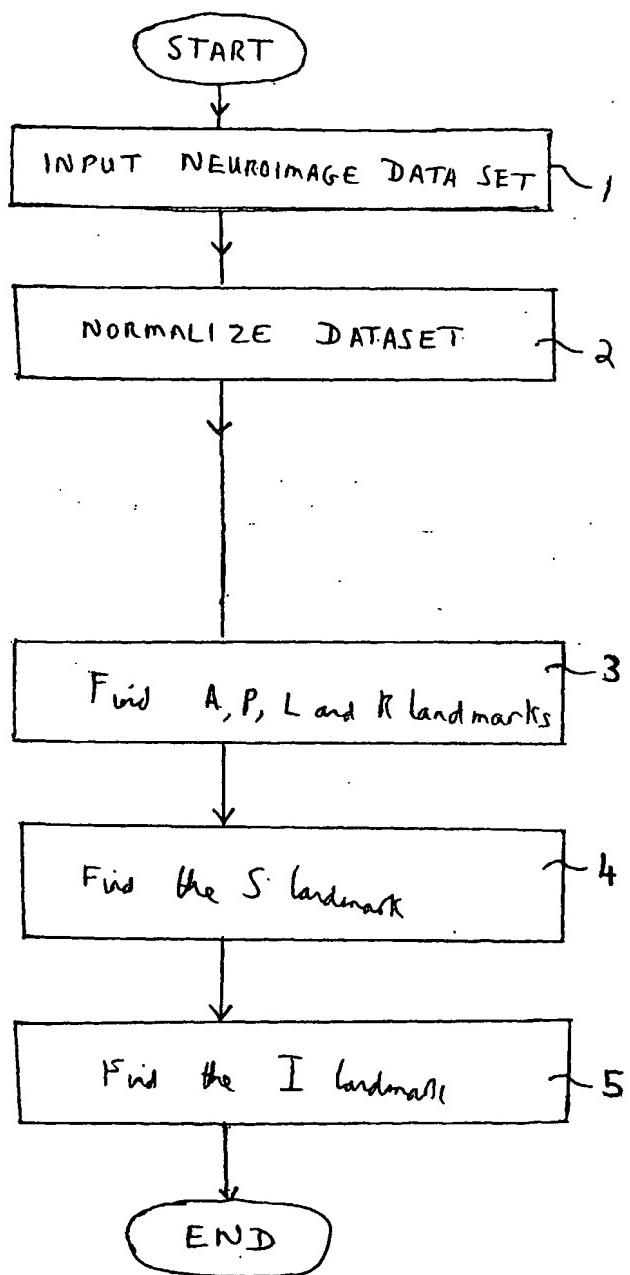


Fig. 1

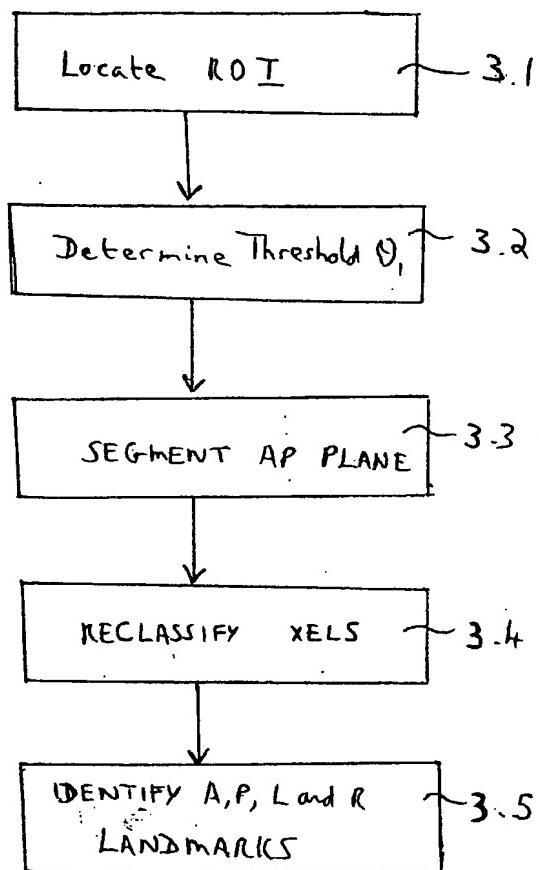
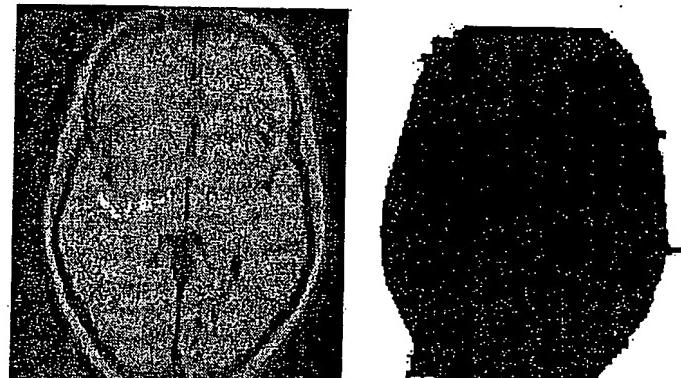
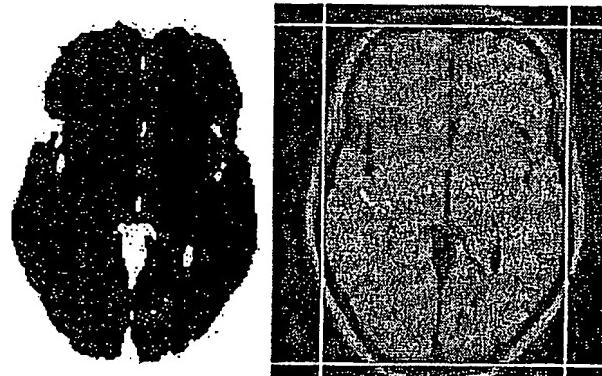


Fig. 2



a)

b)



c)

d)

Fig. 3

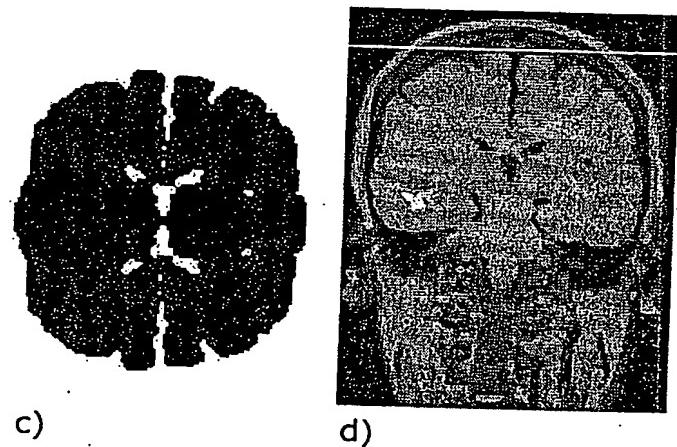
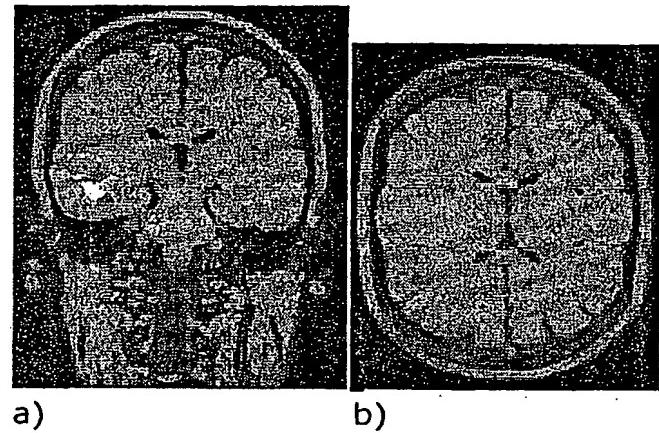
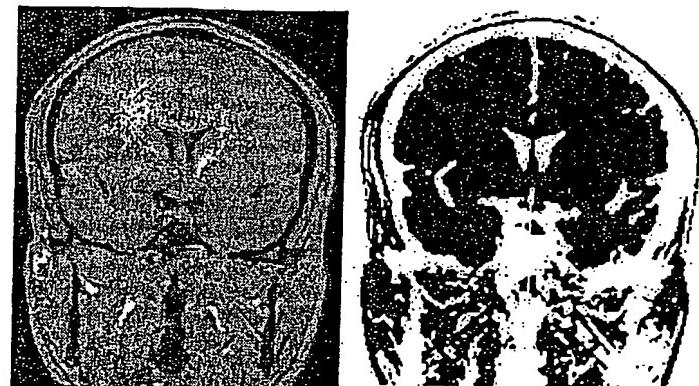
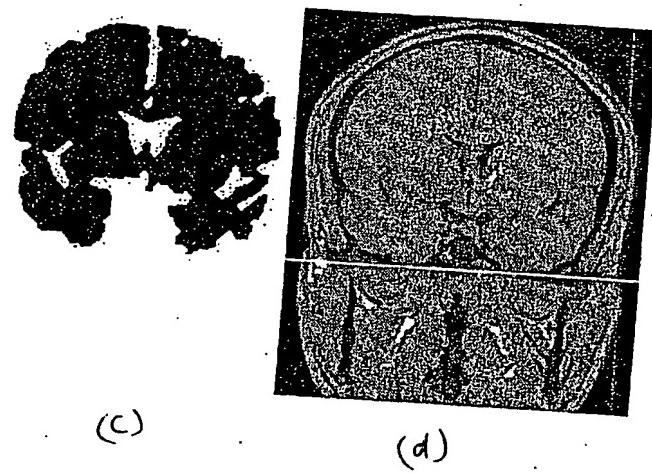


Fig. 4



(a)

(b)



(c)

(d)

Fig. 5

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/SG2004/000219

| <b>A. CLASSIFICATION OF SUBJECT MATTER</b>   |   |  |
|--|---|--|
| Int. Cl. <sup>7</sup> : G06T 3/00  |   |  |
| According to International Patent Classification (IPC) or to both national classification and IPC  |   |  |
| <b>B. FIELDS SEARCHED</b>  |   |  |
| Minimum documentation searched (classification system followed by classification symbols)  |   |  |
| Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  |   |  |
| Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)<br>USPTO, DWPI, internet (landmark, talairach, registration, brain, voxel, mri, partial volume, etc.)   |   |  |
| <b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>  |   |  |
| Category*  | Citation of document, with indication, where appropriate, of the relevant passages                      | Relevant to claim No.  |
| A  | WO 02/43003 A1 (KENT RIDGE DIGITAL LABS), 30 May 2002<br>the whole document (section 2.3 in particular) | 1-21   |
| A  | US 6,408,107 B1 (MILLER et al), 18 June 2002<br>the whole document                                      | 1-21   |
| A  | WO 03/060827 A1 (KENT RIDGE DIGITAL LABS), 24 July 2003<br>the whole document                           | 1-21   |
| <input type="checkbox"/> Further documents are listed in the continuation of Box C <input checked="" type="checkbox"/> See patent family annex   |   |  |
| * Special categories of cited documents:<br>"A" document defining the general state of the art which is not considered to be of particular relevance<br>"E" earlier application or patent but published on or after the international filing date<br>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)<br>"O" document referring to an oral disclosure, use, exhibition or other means<br>"P" document published prior to the international filing date but later than the priority date claimed |   |  |
| Date of the actual completion of the international search<br>16 September 2004   |   | Date of mailing of the international search report<br>21 SEP 2004                      |
| Name and mailing address of the ISA/AU<br>AUSTRALIAN PATENT OFFICE<br>PO BOX 200, WODEN ACT 2606, AUSTRALIA<br>E-mail address: pct@ipaaustralia.gov.au<br>Facsimile No. (02) 6285 3929   |   | Authorized officer<br><br><b>MATTHEW HOLLINGWORTH</b><br>Telephone No : (02) 6283 2024 |

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International application No.  
**PCT/SG2004/000219**

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

| Patent Document Cited in<br>Search Report |          | Patent Family Member |          |    |          |             |
|---|----------|----------------------|----------|----|----------|-------------|
| WO  | 0243003  | AU                   | 15678/01 | EP | 1344187  |             |
| US  | 6408107  | AU                   | 13837/99 | AU | 35911/97 | AU 44244/99 |
|   |          | AU                   | 76019/00 | CA | 2260085  | CA 2308499  |
|   |          | CA                   | 2334272  | EP | 0910832  | EP 1057137  |
|   |          | EP                   | 1086440  | EP | 1222608  | US 6009212  |
|   |          | US                   | 6226418  | US | 6553152  | US 6611630  |
|   |          | US                   | 6633686  | WO | 0122352  | WO 9801818  |
|   |          | WO                   | 9924932  | WO | 9964983  |             |
| WO  | 03060827 | NONE                 |          |    |          |             |

Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.

END OF ANNEX